Modeling and Cumulative Risk Assessment: Case Study for the N-Methyl Carbamate Pesticides

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The Food Quality Protection Act of 1996 (PL 104-170: 110 STAT. 1513) requires EPA to consider potential cumulative human health risks resulting from aggregate exposure to pesticide chemicals acting through a common mechanism of toxicity. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. In 2001, EPA established the N-methyl carbamate pesticides as a common mechanism group based on their similar structural characteristics and shared ability to inhibit acetylcholinesterase (AchE), a critical chemical in the transmission of nerve impulses. EPA's Office of Pesticide Programs (OPP), National Health and Environmental Effects Laboratory (NHEERL and National Exposure Research Lab (NERL), and the CIIT Centers for Health Research are collaborating to develop a physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) model for the N-methyl carbamate pesticides. PBPK/PD models are very powerful tools that can account for anatomic structure and physiological and biochemical processes. These models can be used to estimate internal exposure dose or concentrations of parent compounds and/or active metabolites at the target site(s) and estimate toxicologically relevant effects. Typically, inhibition of AChE is fairly rapid (within hours) for members of the N-methyl carbamate common mechanism group. The time-dependant relationship between exposure and effect for this group make the N-methyl carbamates a good case study to aid the EPA in developing a multichemical, multipathway PBPK/PD model for evaluating cumulative risk. The Office of Pesticide Programs expects to release a preliminary cumulative risk assessment for the N-methyl carbamate pesticides in the spring of 2005. OPP is currently evaluating which method or methods will be used to estimate cumulative risk.